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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,018	10/12/2000	Philip Gotwals	A018	6239

7590

07/30/2002

Biogen Inc
14 Cambridge Center
Cambridge, MA 02142

EXAMINER

ANDRES, JANET L

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 07/30/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/423,018

Applicant(s)

GOTWALS ET AL.

Examiner

Janet L Andres

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 May 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 8,9 and 11-21 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 5 is/are allowed.
- 6) ☒ Claim(s) 1-4,6,7 and 10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7,8.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, polypeptides, in Paper No. 13 is acknowledged. The restriction requirement of paper no. 11 is made FINAL. Claims 1-21 are pending in this application. Claims 8, 9, and 11-21 are withdrawn from consideration as being drawn to a non-elected invention.

Specification

2. The disclosure is objected to because of the following informalities: There are blank spaces on p. 30 where the accession number and name of the deposit have not been filled in. In addition, the ATCC is now located in Manassas, VA.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for TGF- β RII/Fc fusion proteins of SEQ ID Nos: 8 and 9, does not reasonably provide enablement for all TGF- β R fusion proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working

examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte Forman*, (230 USPQ 546 (Bd Pat. App. & Int. 1986)); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988). Claims 1-3 and 10 are broadly drawn and encompass all TGF- β R proteins, including proteins not yet known in the art. Claims 1, 2, and 10 additionally encompass proteins comprising any other protein. In addition, these claims require the ability to inhibit binding of "TGF- β " to a receptor. Applicant has not, however, provided sufficient guidance for one of skill in the art to make and use the proteins as broadly claimed. Massagué (Ann. Rev. Biochem. 1998, vol. 67, pp. 753-791) teaches that TGF- β receptors have different binding properties: the type I receptor, which these claims encompass, cannot bind TGF- β s independently of the type II receptor (p. 762). Further, TGF- β 2 binds the type II receptor weakly in the absence of the auxiliary receptor betaglycan (Massagué, p. 763). Thus, one of skill in the art could not predictably use all molecules potentially within the scope of the claims to bind all forms of TGF- β and to bind them with sufficient affinity to inhibit binding to other receptors. While TGF- β binding regions are known in the art, there is no guidance in the instant specification as to what insertions or deletions would maintain sufficient binding to be useful, and what possible variants would not meet the limitations of the claims. Thus one of skill in the art would require additional guidance, such as information as to what structural features would result in inhibition of TGF- β interaction with other receptors, in order to practice the invention commensurate with the scope of the claims. Furthermore, claims 1, 2, and 10 encompass all fusion partners. There is no indication as to what additional molecules other than immunoglobulins could be used without affecting the ability of the molecule to bind TGF- β , and

no direction as to how one of skill in the art might determine what other molecules could be used. Thus, without further direction as to what molecules might be predicted to fall within the scope of the claims, it would require undue experimentation for one of skill in the art to make and use the invention as broadly claimed.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 1-4, 6, 7, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lin et al., U.S. patent 6046157, filed 1995 in view of Jacobs et al., U.S. patent 5605690, 1997.

Lin et al. teaches methods using soluble TGF β RII receptors to inhibit TGF β function (see claims, columns 37-40). Lin et al. fails to teach Fc fusion proteins. However, such fusion proteins are taught by Jacobs et al. for soluble TNF α receptors (see figures 1 and 3-6, columns 2, 7, 19, and 20, for example). Jacobs et al. fails to teach TGF β RII fusion proteins. However, it would have been obvious to one of ordinary skill in the art to combine the teachings of Lin et al.

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with those of Jacobs et al. to produce such fusion proteins. One of ordinary skill would have been motivated to do so because Lin et al. teaches the use of soluble TGF β RII receptors to lower TGF β levels, and Jacobs et al. teaches the use of such fusion proteins in an analogous system, soluble TNF α receptors, for use in lowering TNF α levels, and teaches that such fusion proteins are effective and may have particular advantages (column 7, lines 52-54). Thus, one of ordinary skill would have expected such a fusion protein to be able to inhibit TGF β function.

CLAIMS 1-4, 6, 7, AND 10 ARE REJECTED. CLAIM 5 IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 872-9306 or (703) 872-9307 for after final communications.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly

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set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.
July 25, 2002


YVONNE EYLER, PH.D.
SUPERVISORY PATENT EXAMINER
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